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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,296	09/30/2003	Lance G. Laing	04107/100L443-US2	8464

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EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,296	LAING, LANCE G.	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/30/03, 11/26/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a supplemental IDS filed 11/26/2003.

Claims 1-2 are pending in the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in that the metes and bounds of the phrase "portion of an ArsR protein consisting of" are unclear. It is unclear whether the phrase specifies (i) a portion or fragment of a protein of any length that is 90% identical to amino acids 1-97 of SEQ ID NO: 2 or (ii) a portion of the ArsR protein of the claim that has 90% identity over the entire length of SEQ ID NO: 2. It would be remedial to amend the claim language to distinctly claim the intended structural/functional features of the ArsR protein.

Claim 2 is vague and indefinite in that the metes and bounds of the term "has" are unclear. The term "has" can be interpreted as "consisting of" or "comprising". It would be remedial to amend the claim to use either open or closed language.

Claim 2 is vague and indefinite in that the metes and bounds of the term "an amino acid sequence" are unclear. The term "an amino acid sequence" can be broadly interpreted as encompassing any amino acid sequence within amino acids 1-97 of SEQ ID NO: 2.

Alternatively, the term could be interpreted as "the" amino acids 1-97 of SEQ ID NO: 2. It would be remedial to amend the claim language to distinctly claim the intended structural/functional features of the ArsR protein.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 2 are drawn to an ArsR protein comprising a portion of an ArsR protein consisting of an amino acid sequence that is at least 90% identical to the amino acid sequence of amino acids 1-97 of SEQ ID NO: 2, which ArsR protein binds to a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 3, 4, 5, 6, 7, 8, 9, and 10, and the claimed ArsR protein which has an amino acid sequence of amino acids 1-97 of SEQ ID NO: 2. The claims are interpreted broadly as encompassing a fragment of a protein that is 90% identical to any amino acids within residues 1-97 of SEQ ID NO: 2 or a portion of the ArsR protein that has 90% identity to residues 1-97 of SEQ ID NO: 2. Thus, the claims can be interpreted to encompass literally any ArsR protein having only a portion of an ArsR protein sequence found in SEQ ID NO: 2 (e.g. any dipeptide of SEQ ID NO: 2). Even if one interprets claim 1 as being

limited to proteins comprising a portion of itself having 90% identity to SEQ ID NO: 2, the rejected claims encompass embodiments where at least 9 changes can be made within 1-97 of SEQ ID NO: 2, and further, where additional protein sequences can be present flanking the portion of the ArsR protein that has 90 % identity to SEQ ID NO: 2. Moreover, the proteins encompassed by the claims must function as an ArsR protein (i.e. "an ArsR" protein) and must be able to bind specific DNA sequences (i.e. SEQ ID NOS: 3-10). Therefore, the rejected claims encompass an enormous genus of proteins that must retain very specific functional properties.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the product and any combination thereof. The specification discloses SEQ ID NO: 2, a 117 amino acid ArsR protein from *E. coli*. The specification describes codon optimization and subcloning of the ArsR coding sequence into a plasmid which contains a His6 carboxy terminal tag to provide a source of full-length ArsR protein (Example 1). The specification discloses a partial structure in the form of a recitation of percent identity where the protein must be capable of binding specific DNA sequences (e.g. page 33, lines 15-18). The only variants described in the specification are the deletion of residues 98-117 to make the protein less susceptible to aggregation/precipitation and deletion of residue 116 to increase the stability of the protein (e.g. page 33, lines 5-15; page 42, lines 24-25). No description is provided of any other variant of SEQ ID NO: 2. The distinguishing characteristics of the claimed genus are not described. The specification does not identify any particular portion of the ArsR protein structure that must be

conserved, nor does it describe structure/function correlation. With regard to the functional characteristics of the ArsR protein, the specification describes complementary oligonucleotide sequences of the *ars* operon from either a plasmid or chromosome in certain bacteria (e.g. page 42, lines 28-30; page 43, lines 1-3; Table 2) and describes the binding of ArsR protein to the immobilized double stranded oligonucleotides in the presence and absence of phenlyarsine oxide (Example 2). The protein-DNA binding affinities were different for each oligonucleotide sequence used (page 44, lines 11-13). However, no description is provided of the effect of sequence alterations in the amino acid sequence of SEQ ID NO: 2 on binding affinity for any of the target nucleic acids. The specification provides no guidance with regard to which residues within SEQ ID NO: 2 might be essential for specific DNA binding. Therefore, no active variants are disclosed.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe a set of ArsR proteins comprising a portion of an ArsR protein consisting of an amino acid sequence that is at least 90% identical to the amino acid sequence of amino acids 1-97 of SEQ ID NO: 2, which ArsR protein binds to a nucleic acid sequence selected from the group consisting of SEQ ID NOS: 3-10. The ArsR family of proteins requires at least three protein domains to function (i) a metal binding domain, (ii) a DNA binding domain, and (iii) a dimerization domain (Xu et al, The Journal of Biological Chemistry, Vol. 272, No. 25, pages 15734-15738, 1994; e.g. Introduction). Shi et al (The Journal of Biological Chemistry, Vol. 269, No. 31, pages 19826-19829, 1994) define the metal binding domain of ArsR proteins as encompassing amino acids 30 to 36 (ELCVCDL) of the ArsR protein from *E. coli* plasmid R773 (e.g. Introduction). Further, Shi et al demonstrate that ArsR mutants (C32Y, C32F and C34Y)

are able to specifically bind the *ars* promoter but have a reduced inducer response to a metal compound (e.g. Figure 5). Wu et al (Molecular Microbiology, Vol. 5, No. 6, pages 1331-1336, 1991) describe ArsR proteins comprising amino acids 1-102 that are able to bind the *ars* promoter whereas proteins comprising amino acids 1-83 were unable to bind DNA (e.g. Table 1). Xu et al (1997) define the region of the ArsR protein required for dimerization as residues 9-89 (e.g. Figure 1). Though a broad localization of the functional domains of the ArsR proteins has been described in the prior art, the specific structure/function correlation of residues essential for specific DNA binding has not been described. Further, natural variation in ArsR sequences known in the prior art does not make up for deficiencies in the specification. For example, the *E. coli* chromosomal *arsR* gene encodes a protein that is 75% identical to that of the *E. coli* R773 repressor but only 26% identical to the staphylococcal plasmid pI258 or pSX267 ArsR proteins (Xu et al, The Journal of Biological Chemistry, Vol. 271, No. 5, pages 2427-2432, 1996; e.g. Introduction). Though sequence variation is present in ArsR proteins, the specific changes in SEQ ID NO: 2 which would allow specific binding to the *ars* promoter have not been described in sufficient detail as to provide a structural/functional basis for envisioning the broadly claimed genus of proteins.

Given the very large genus of proteins encompassed by the rejected claims, and given the limited description provided by the prior specification with regard to the modifications that can be made to SEQ ID NO: 2 and still retain functional activity, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of proteins. Therefore, the skilled

artisan would have reasonably concluded applicants were not in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al (Molecular Microbiology, Vol. 5, No. 6, pages 1331-1336, 1991; see the entire reference.

Wu et al teach the amino acid sequence of an arsenical resistance operon repressor from *E. coli* plasmid R773 (e.g. Figure 2). The disclosed sequence is contained in GenBank accession number P15905. The amino acid sequence from amino acids 1-97 of accession number P15905 is 100% identical to positions 1-97 of SEQ ID NO: 2 (alignment provided) and therefore comprises a protein of positions 1-97 of SEQ ID NO: 2.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jennifer Dunston
Examiner
Art Unit 1636

jad

GERRY LEFFERS
PRIMARY EXAMINER